REMARKS

Claims 35-53 are pending in this application. Claims 35-39 and 53 stand rejected. Claims 40-52, 54, and 55 have been withdrawn from consideration as being drawn to the non-elected invention. None of the claims stand objected to. Claims 35, 36, 38, and 53 have been amended. Support for these claims can be found in the as-filed claims and specification. Accordingly, these amendments introduce no new matter.

In view of the following amendment and response, the Applicants believe the claims presented hereln are allowable. Reconsideration is respectfully requested.

SEQUENCE COMPLIANCE

The Examiner has noted that Figures 3, 4, and 9 (pages 9/15 and 10/15) of the instant specification recite nucleotide/amino acid sequences which are encompassed by the definitions for nucleotide sequences as set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). The Examiner notes that the sequence identifier must still be used, either in the drawing or in the Brief Description of the Drawings when a sequence is presented in a drawing. Applicants have corrected this error and have added the appropriate sequence identifiers to the sequences mentioned in Figures 3, 4 and 9.

In view of the foregoing, Applicants believe the instant specification now complies with all relevant sequence rules.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 35-39, and 53 have been rejected under 35 U.S.C. § 112, second paragraph for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention.

The Examiner states:

> *Claim 35 is vague and indefinite because it is unclear what structure is being claimed. The Claim allows for a 20% difference in the recited sequences. It is unclear what structures are encompassed by this Claim. The metes and bounds of the claim cannot be understood.*

First, amendments have been made to claim 35 to add the phrase "at least" to make the intent of the Applicants clearer. Secondly, without acquiescing to any bases of rejection, but purely to expedite the prosecution of the case, additional amendments were made to limit the scope of claim from 80% to 90% identity. Support for such amendments can be found under the heading **Polynucleotides of the Invention** on page 16, line 20 to page 17, line 4.

"Identity" is a degree of similarity after two sequences are compared, and it is widely used in the art to compare sequences. In general, the sequences are aligned so that the highest order of match is obtained. The specification from page 11, line 19 to page 12, line 21 teaches clearly what is meant by "identify" as used in the claim. It is submitted that metes and bounds of claim 35 as defined by "identify" is clear.

The Examiner states Claim 36 is vague and indefinite due to the phrase "recombinant expression system". She questions:

> *What is encompassed by this terminology? Is this an expression vector comprising the polynucleotides of Claim 35?*

Attention is invited to page 20, lines 3-15 where "expression system" as used in the claim is defined. It is believed that the definition of expression system contained therein obviates any issue of alleged vagueness. In addition, claim 36 has been amended to clarify that the polynucleotide of claim 35 is contained in a recombinant expression system.

The Examiner further alleges that Claims 38 and 39 are vague and indefinite because it is unclear how a polynucleotide sequence which varies by 20% will have the capability of producing a LbpB polypeptide. She states that the specification is silent as to the nucleotide changes which can be made to the defined sequences and still produce a functional protein.

Applicants respectfully disagree with the Examiner on this issue. Those having ordinary skill in the art know that, due to the degeneracy of the code, two polynucleotide sequences having as little 60% identity to one another may nevertheless encode for the same polypeptide sequence (i.e. 100%

homologous), let alone the instant claims are now limited only to at least 90% identity (see "Wobble hypothesis", Lewin, B., Genes IV, pp. 144-150 (1990)).

Further, it is within the common general knowledge of the skilled person to realize that some amino acid changes are conservative in nature, so for instance, a change from a lysine to an arginine residue would be unlikely to disrupt the structure of a protein hence a change from a AAG to a AGA codon should still fall within the scope of the claims. Moreover, figure 9 of the application teaches that some amino acids are conserved in all five sequences whereas other amino acid residues can be changed without affecting the activity of the LbpB. For instance amino acids 160-162 of the BNCV LbpB sequence could be changed from KWT to EWT or EQN without affecting the activity of the LbpB. It is also important to alert the Examiner that percentage identity among the five sequences provided in figure 9 are already roughly 55-60%. Hence the skilled person could easily design polynucleotides encoding LbpB with sequences up to at least 90% different from any of the precise sequences disclosed by following the teaching of Figure 9.

The Examiner has suggested that Claim 38 should be amended to recite "A process for producing a 'host' cell" in order to clarify that it is a transformed cell which is being produced.

The Examiner has also suggested that Claim 53 should be amended to a kit comprising an " 'isolated' polynucleotide." Amendments have been made to claims 38 and 39 as suggested by the Examiner.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 35-39, and 53 stand rejected under 35 U.S.C. § 112, first paragraph, allegedly because the specification, while being enabling for "an isolated polynucleotide encoding *Neisseria meningitides* LbpB selected from the group consisting of SEQ ID NO:1 (nucleotide 100-nucleotide 2274), SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, or SEQ ID NO:9' and for an isolated polynucleotide which encodes the amino acid sequence set forth in SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, or SEQ ID NO:10' and host cells and test kits comprising the

polynucleotide sequences, does not reasonably provide enablement for "An isolated polynucleotide encoding a Neisseria meningitides LbpB protein, selected from the group consisting of: an isolated polynucleotide sequence that it at least 80% identical to that of SEQ ID NO:1 (nucleotide 100-nucleotide 2274), SEQ ID NOs: 3, 5, 7, or 9", nor is it enabled for methods of making a protein using these polynucleotides for test kits for diagnosing neisserial bacteria in a human which comprise these polynucleotide. The Examiner states, inter alia,

> *The breadth of the instant claims contain nucleotide sequences other than what is specified in the sequence disclosure. The specification states that substitutions, additions, or deletions may be made to the defined sequences; however, the specification provides no guidance as to what nucleotides may be changed without causing a detrimental effect to the protein to be produced. Further, it is unpredictable as to which nucleotides could be removed and which could be added....*
>
> *A nucleotide sequence with 20% random difference may very well lose the ability to bind to a human lactoferrin as required by the claims and is unlikely to produce a functional LbpB polypeptide as required by claims 36-39. Additionally, a polynucleotide sequence with a 20% difference will not function as a reliable detection agent in a kit for diagnosing infection with neisserial bacteria. To start with the DNA sequence first, this requires even more work on the part of the skilled artisan.*
>
> *Applicants have provided no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different nucleotide substitutions and the nature and extent of the changes that can be made. Given the lack of guidance contained in the specification and the unpredictability for determining acceptable nucleotide substitutions, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.*

As the Examiner fully appreciates enablement requirement is still met even if a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404. As stated above Applicants did provide enough guidance to enable one of ordinary skill how to determine, without undue experimentation, ways to retain the property of LbpB polypeptides. Once again, figure 9 of the application teaches that some amino acids are conserved in all five sequences whereas other amino

acid residues can be changed without affecting the activity of the LbpB. For instance amino acids 160-162 of the BNCV LbpB sequence could be changed from KWT to EWT or EQN without affecting the activity of the LbpB. Hence the skilled person can design polynucleotides encoding LbpB with sequences up to at least 90% identity difference from any of the precise sequences even with some undue experimentation. The specification supplies enough guidance with respect to the direction in which the experimentation should proceed.

CLAIM REJECTION – 35 USC 112- WRITTEN DESCRIPTION

Claims 35-39, and 53 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner states, *inter alia,*

> *The written description in this case only set forth SEQ ID NO:1 (from nucleotide 100 to nucleotide 2274), 3, 5, 7, and 9 and equivalent degenerative codon sequences thereof, i.e., isolated polynucleotides encoding the amino acid sequence set forth in SEQ ID Nos: 2, 4, 6, 8, or 10, and therefore the written description is not commensurate in scope with the claims which are broadly drawn to any isolated polynucleotide encoding N. meningitides LbpB (claim 35) and polynucleotides which vary by 20% of the known sequences...*
>
> *....Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID Nos: 1 (from nucleotide 100 to nucleotide 2274), 3, 5, 7, and 9 and the degenerates thereof, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolated. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.*
>
> *Furthermore, in The Reagents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to*

disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA ... ' requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention."

Applicants respectfully disagree with the Examiner on the following grounds. The Examiner cites The Reagents of the University of California v. Eli Lilly (herein afterward The Reagents) for the proposition that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide adequate written description of the genus. However, the Reagents case can be clearly distinguished from the instant case because the Applicants are not defining the polynucleotides in terms of functional activity but in terms of "identity." As stated earlier, a skilled person can clearly understand what is meant by polynucleotides having at least 90% identity to SEQ ID NOs: 1, 3, 5, 7 or 9. Defining polynucleotides in terms of "identity" is describing sequences using a mathematical algorithm which is equivalent to precisely defining the DNA in terms of "structure, formula, chemical name, or physical properties" that the Reagent court required. Moreover, as Examiner acknowledges, Applicants are not required to disclose every species encompassed by the genus, and the description of a genus is achieved by the recitation of a representative number of DNA molecules. To this end, Applicants have already disclosed five representative examples of LbpB polypeptides in Figure 9. Thus it is respectfully submitted that Applicants were in clear possession of the claimed subject matter.

The Examiner makes the statement that no disclosure beyond the mere mention of allelic variants is made in the specification. The allegation made by the Examiner is erroneous. For the record, what are listed in figure 9 are not simple allelic variants, but LpbB polypeptides from different species.

The Applicants respectfully submit that, in view of the forgoing remarks, Applicants have addressed all the issues raised by the Examiner, and have overcome the Examiner's rejection of

Claims 35-39, and 53. Accordingly, favorable reconsideration and allowance of the pending claims is earnestly solicited. If it would expedite the prosecution of this application, the Examiner is invited to confer with the Applicants' undersigned attorney.

Respectfully submitted,

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